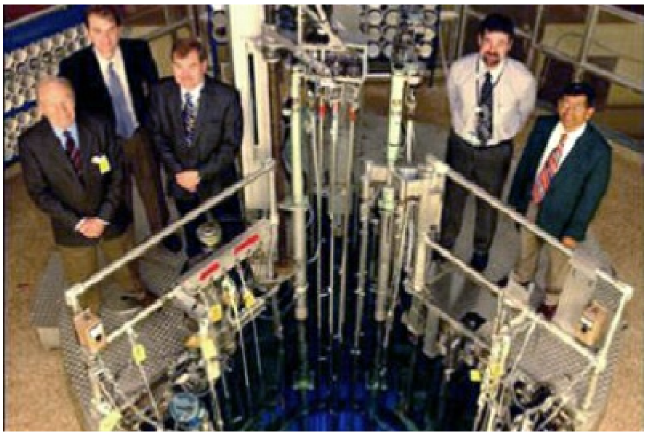


Dr. Fred Hawthorne (left) and colleagues at the University of Missouri Research Reactor are part of a new collaboration with INL to revitalize Boron Neutron Capture Therapy research for controlling head and neck tumors.

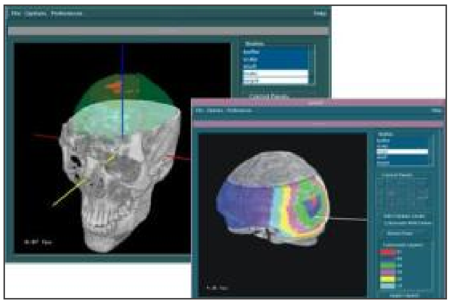
INL partners revitalizing BNCT research

by Megan Crepeau, *Nuclear Science & Technology Communications*

As cancers go, glioblastoma multiforme is just about as bad as it gets.

It is the most lethal form of brain cancer. Less than 10 percent of patients can expect to survive more than a year after diagnosis. Tumors sprout anywhere in the brain and grow quickly once they have taken hold, spreading themselves throughout the brain, destroying normal function. Symptoms, including nausea, headaches, seizures and memory loss, often do not appear until the tumor has grown very large. The disease has no known cause. It has proven particularly resistant to conventional treatments.

There might be hope, though, and it might be coming from right here in Idaho. Idaho National Laboratory researchers have teamed up with the University of Missouri (MU) and Washington State University to revitalize Boron Neutron Capture Therapy (BNCT) research, seeking an effective means of controlling certain other, more common, types of head and neck tumors that would otherwise require disfiguring surgery, or simply fail to respond to traditional cures. This perhaps could be followed by new approaches to glioblastoma, a traditional target of BNCT research, said INL physicist David Nigg, Ph.D.



Calculated dose distribution on a reconstructed medical image produced by INL's SERA computational dosimetry software package developed in collaboration with Montana State University.

Nigg has studied BNCT since the 1980s and has led the lab's radiotherapy research, sponsored by the U.S. Department of Energy Office of Science, since 1994. Now, with new partners and a renewed interest from INL in reinvigorating BNCT research, he and his colleagues hope to make BNCT a customary option for one or more difficult diseases.

"We have not been as active recently as we used to be," Nigg said. "Over the past two or three years, the DOE has been re-evaluating its position (on nuclear medicine research)."

BNCT is a process that aims to eliminate tumors through nuclear technology. First, boron-10 is attached to a "delivery agent" that is attracted to tumor cells. Patients swallow or are injected with the agent, which attaches itself to the tumor. Then, technicians aim a concentrated beam of neutrons at the tumor. When the neutrons collide with the boron, the boron atoms release radiation in the form of an alpha particle and a lithium ion. That radiation travels only far enough to destroy the cells it is in – ideally destroying the tumor from the inside without adversely affecting healthy tissue.

Radiation therapy has been part of cancer treatment for almost 100 years, and scientists have been intrigued by the idea of neutron capture therapy since 1936. In the United States, the first human trials of BNCT started in the 1950s – and ended shortly thereafter, largely due to lack of suitable technology. In Japan, however, experimenting continued, with encouraging results and improved technology that jump-started a new wave of attention to BNCT in the late 1980s. New human trials in the U.S. took place in the 1990s, with technical support from INL.

Today, the treatment is relatively common in Japan and in a few other countries, especially Finland. Closer to home, Nigg and his INL team are collaborating with the University of Missouri to help BNCT regain a foothold in the states, with an emphasis on new tumor types and significantly improved boron agents compared to those of the 1990s.

One of the main roadblocks to that goal was overcome in the 1990s when INL scientists found a better way to synthesize decaborane, a key precursor to one of the current FDA-approved delivery agents called GB-10. INL's advances in support of GB-10 production enabled the manufacture of enough for research use, which has led to some significant new insights into the radiobiology of BNCT over the past few years. Bill Bauer, Ph.D., and his colleagues at INL have also made key contributions to the technology and protocols for measuring boron in tissue. All of this experience, in addition to INL's extensive experience in neutron source design and dosimetry for BNCT, will permit the INL to contribute to the collaboration with MU in a very proactive manner.

Help has come from overseas as well. Since 2001, a collaboration between INL researchers and

INL scientists Dave Nigg (4th from right) and Bill Bauer (right) with Dr. Mario Pisarev (left) and Dr. Amanda Schwint (3rd from left) and their colleagues at the Argentine research reactor laboratory RA-1 in Buenos Aires.

some of their counterparts at the National Atomic Energy Commission of Argentina has proven fruitful. In 2003, the Argentine team began conducting human trials of BNCT and helped jump-start small-animal testing of GB-10, in collaboration with INL. The Argentine researchers have also joined forces with MU and INL in the latest collaboration, making current BNCT research a truly global initiative.

Nigg admits that BNCT research is a "niche" area for the INL, and it is not his only area of research at the laboratory. He and his colleagues also work on more traditional INL pursuits such as reactor technology. Though the nuclear medical specialty may be small, he is proud of its tradition at INL, pointing out that in addition to INL contributions to BNCT research over the years, the lab's Advanced Test Reactor produces radioisotopes for medical research. Also, a team of INL radiochemistry researchers has developed a new process that could be used to extract certain useful medical radioisotopes from the DOE stockpile of excess uranium-233.

"We are invested in nuclear medicine," he said.

The new MU partnership is a significant part of that investment. MU has a well-regarded research reactor and a tie to INL in Dr. Fred Hawthorne, a longtime INL collaborator and world-famous boron chemist and nominee for the Nobel Prize who is now so well-established at MU that the school has given him his own thermal neutron beam line – one that INL helped design and produce – for BNCT research. Now, with a recent startup of a new Laboratory Directed Research and Development project at INL, the Idaho team can hit the ground running in partnership with Missouri researchers to take the next steps. Nigg said that the partners hope to start testing on small animals – rats and/or mice – within the next few months.

After that, the next natural step would be tests on larger animals, most likely dogs, whose tumors are biologically much closer to those of humans, Nigg said. This would be done at Washington State University, where INL has con-structed a neutron beam more appropriate for large animals. The team hopes to be ready for initiation of new human trials within five years, again at the University of Missouri, where a suitable neutron source would be constructed in parallel with the ongoing animal research. Then would come FDA approval and, ideally, BNCT's acceptance into the American medical mainstream.

This collimator assembly for the BNCT neutron beam was constructed at Washington State University's TRIGA research reactor facility. The INL Prototype Shop fabricated many of its complex bismuth parts.

If things go as planned, it would be the culmination of many years' work for Nigg, who views the research as more than just a vocation.

"This has been a strong personal interest of mine," he said. "It is a fascinating application of nuclear science that has great potential to make a difference in people's lives."

[Feature Archive]